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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/142,970	04/02/1999	MARK ACHTMAN	7101/0E616	2916

7590 01/31/2002

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EXAMINER
GRASER, JENNIFER E

ART UNIT	PAPER NUMBER
1645	13

DATE MAILED: 01/31/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/142,970	Achtmann et al.
Examiner	**Art Unit**
Jennifer Graser	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Amendment B, 11/21/02* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *26-50* is/are pending in the application.

4a) Of the above, claim(s) *42-50* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *26-41* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

1. Acknowledgment and entry of the Amendment submitted 11/21/01, Paper No. 12B is made. Claims 26-41 are currently under examination.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 26-41 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 26, 27, 29, 30, and 32-41 are vague and indefinite because it is unclear what is encompassed by the term "homologous". It is unclear what level of homology is shared between the peptide and those peptides identified by SEQ ID NO. . The term "homologous" reads on a fragment which shares one amino acid in common. It is unclear how the amino acid sequence can vary without upsetting the function of the polypeptide. Applicants have argued that the definition in the specification recites that the term "homologous refers to a sequence that is at least 80% identical to the respective sequence". This argument has been fully and carefully considered but is not deemed persuasive. While the specification can be used to provide

definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed. Claims 26, 27, 29, 30, and 32-41 merely recite the term "homologous" which can be broadly interpreted as reading on a sequence with as little as one amino acid in common.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 26-41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The breadth of the instant claims contain amino acid sequences other than what is specified in the sequence disclosure. The specification states that substitutions, additions, or deletions may be made to the defined sequences; however, the specification provides no guidance as to what amino acids may be changed without causing a detrimental effect to the protein/peptide to be produced. The specification provides insufficient guidance as to what level of homology and characteristics define homologous. Further, it is unclear how the amino acid

sequence can vary without upsetting the function of the polypeptide. It is unpredictable as to which amino acids could be removed and which could be added. While it is known that many amino acid substitutions are possible in any given protein/peptide, the position within the protein/peptide's sequence where amino acid substitutions can be made with a reasonable expectation of success are limited. Other positions are critical to the protein's structure/function relationship, e.g., such as various positions or regions directly involved in binding, catalysis in providing the correct three-dimensional spacial orientation of binding and catalytic sites. These regions can tolerate only very little or no substitutions. A 1-99% change in the coding region (as is encompassed by the present claims, i.e, the term homologous with no specific percent identity identified) could cause a detrimental effect to the protein/peptide to be produced and could cause total negation of any epitopes which could induce an immune response or much less produce a functional protein or fragment. Additionally, selective point mutation to one key antigen residue could, in practical terms, eliminate the ability of an antibody to recognize this altered antigen. If the range of decreased binding ability after single point mutation of a protein antigen varies one could expect point mutations in the protein antigen to cause varying degrees of loss of protection, depending on the relative importance to the binding interaction of the altered residue. Alternatively, the combined effects of multiple changes in an antigenic determinant could again result in loss of protection. A protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies in the polyclonal pool. It is expensive and

time consuming to make amino acid substitutions in a particular region of a protein in view of the possibilities for change in structure and the uncertainty as to what utility will be possessed.

Applicants have provide no guidance to enable one of ordinary skill in the art how to determine, without undue experimentation, the effects of different amino acid substitutions and the nature and extent of the changes that can be made. Given the lack of guidance contained in the specification and the unpredictability for determining acceptable amino acid substitutions, one of skill in the art could not make or use the broadly claimed invention without undue experimentation.

Response to Applicant's arguments:

Applicants argue that the specification refers to the term "homologous" as a sequence that is 80% identical to the respective sequence. As stated above, many of the claims do not recite a limitation of 80% identity. Instead, they solely claim "homologous" sequences. As stated in the 112, second paragraph rejection set forth above, While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed. Claims 26, 27, 29, 30, and 32-41 merely recite the term "homologous" which can be broadly interpreted as reading on a sequence with as little as one amino acid in common.

Further, Applicants state that they intend for substitutions, deletions and additions to be encompassed by the term "homologous', yet the specification provides no guidance as to what amino acids may be changed without causing a detrimental effect to the protein/peptide to be produced. It is unclear how the amino acid sequence can vary without upsetting the function of the polypeptide. It is unpredictable as to which amino acids could be removed and which could be added. While it is known that many amino acid substitutions are possible in any given protein/peptide, the position within the protein/peptide's sequence where amino acid substitutions can be made with a reasonable expectation of success are limited. Other positions are critical to the protein's structure/function relationship, e.g., such as various positions or regions directly involved in binding, catalysis in providing the correct three-dimensional spacial orientation of binding and catalytic sites. These regions can tolerate only very little or no substitutions. A 1-99% change in the coding region (as is encompassed by the present claims, i.e, the term homologous with no specific percent identity identified) could cause a detrimental effect to the protein/peptide to be produced and could cause total negation of any epitopes which could induce an immune response or much less produce a functional protein or fragment. Additionally, selective point mutation to one key antigen residue could, in practical terms, eliminate the ability of an antibody to recognize this altered antigen. If the range of decreased binding ability after single point mutation of a protein antigen varies one could expect point mutations in the protein antigen to cause varying degrees of loss of protection, depending on the relative importance to

the binding interaction of the altered residue. Alternatively, the combined effects of multiple changes in an antigenic determinant could again result in loss of protection.

With the exception of the proteins and protein fragments of SEQ ID NO:1, 2, 3, 4 and 5, the skilled artisan cannot envision the detailed structure of the encompassed polypeptides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of making it.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 26, 27, 29, 30, and 33-41 are rejected under 35 U.S.C. 102(b) as being anticipated by Kilian et al. (WO/9011367).

Kilian et al recite Iga1 proteases and fragments of the Iga1 proteases. Fragments which are 59.1% homologous to SEQ ID NO:1, 58.6% homologous to SEQ ID NO:2, 56.9% homologous to SEQ ID NO:3, 49.5% homologous to SEQ ID NO:4, and 52.8%homologous to SEQ ID NO:5 are disclosed. See attached sequence alignments. These fragments read on peptides which are 40-200 amino acids length and "homologous" to positions 1 to 5 - 40 to 104

of SEQ ID Nos: 1-5. The instant claims read on sequences which have as few as 1 amino acid in common. Further, the prior art peptides are also Iga1 protein fragments and therefore have a homologous activity. See claim 1 of Patent Serial No. WO/9011367 which recites IgA1 proteases and *fragments thereof.*

Rejections which were overcome:

8. The former rejection of claims 26-41 under 35 U.S.C. 102(b) as being anticipated by Lomholt et al (Mol. Microbiol., 1995, 15: 495-506), Pohlner et al. (Nature. 1997, 325; 458-462), or Meyer et al. (US Patent Serial No. 5,268,270) have been obviated by the amendment of claim 26 to recite "an isolated peptide *consisting of* 40 to 200 amino acids". The prior art references disclosed only the full length sequence of IgA1 protease from *Neisseria* and do not teach or suggest any fragments from the full length protease which is much larger than the instantly claimed fragments.

9. Applicant's amendment to claim 26 necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is (703) 308-4242 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (703) 308-1742. The examiner can normally be reached on Monday-Friday from 7:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JGraser 1/30/02

Jennifer Graser
Primary Examiner
Art Unit 1645